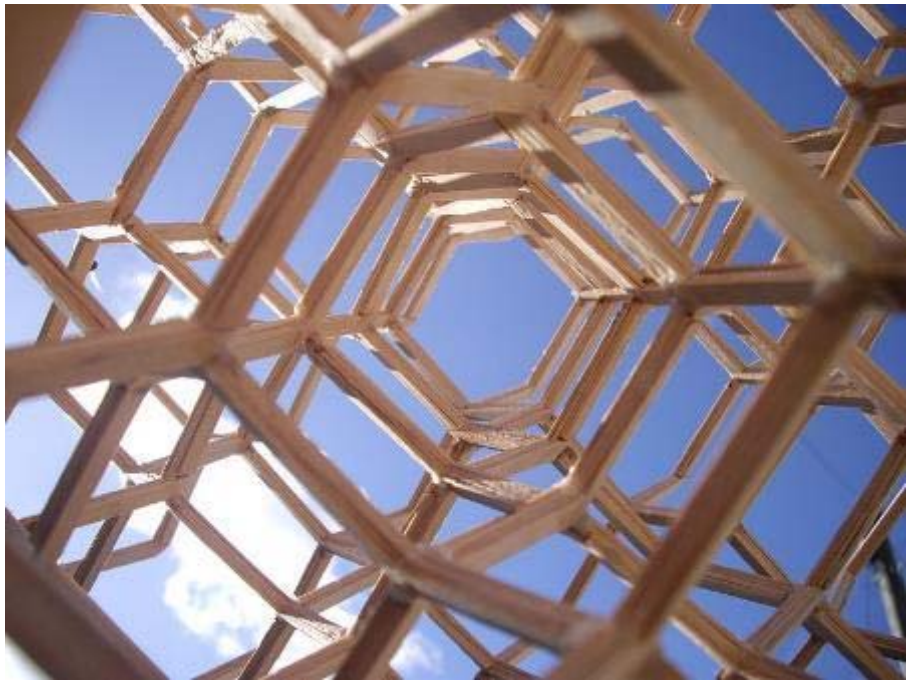
DECISION FRAMEWORKS AND DATA INTEGRATION

Alternatives to Animals for Ecotox Testing Committee

Eco-TTC Framework

Scott Belanger, PhD, P&G



Frameworks for intelligent non-animal testing

Framework development

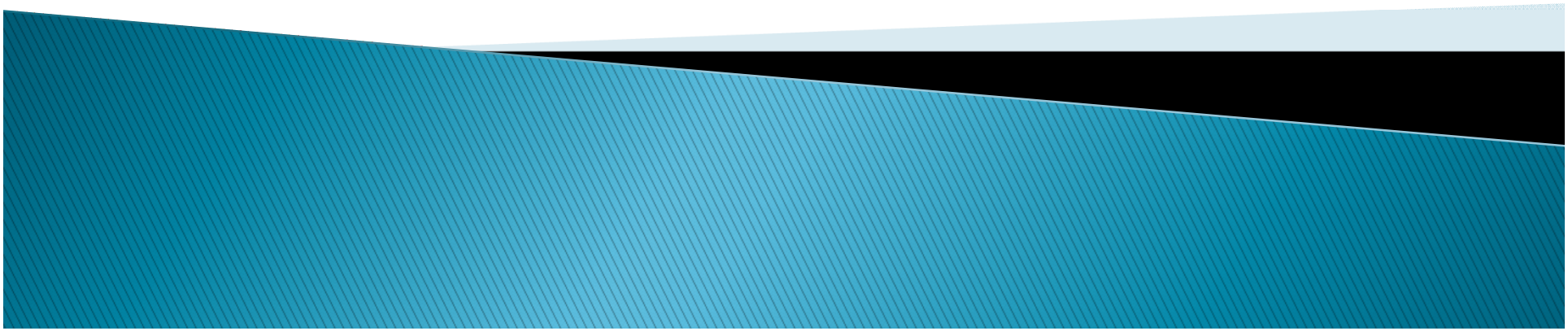
Alan Boobis, PhD, Imperial College

Data Integration in the Development of Ecological Thresholds of Toxicological Concern (eco-TTC)

HESI Animal Alternatives in ERA Committee

Scott Belanger

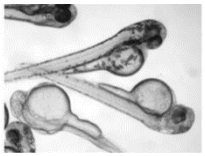
HESI Annual Meeting
7 June 2016



Considerations that differentiate human and environmental risk assessment

- Protection target: all possible species in all types of ecosystems
  - 8.7 million described species
  - 31,000 fish species alone
  - FW, SW, sediment, agricultural land, WWTPs
  - True goal: protection of ecosystem services
    - Energy flow
    - Nutrient flow
    - Biodiversity





- Amount of available data

- Often means product level exposure versus summed exposures from all uses of a chemical, in other words total industry volumes are necessary for assessments and understanding effluents which aggregate many sources

- Exceptional reliance on biostatistics and extrapolation

The world of animal alternatives….

REPLACEMENT

Tier I: a) phys-chem analyses, literature search, read across b) QSARs

Tier II: non vertebrate or *In vitro* assays to evaluate toxicity

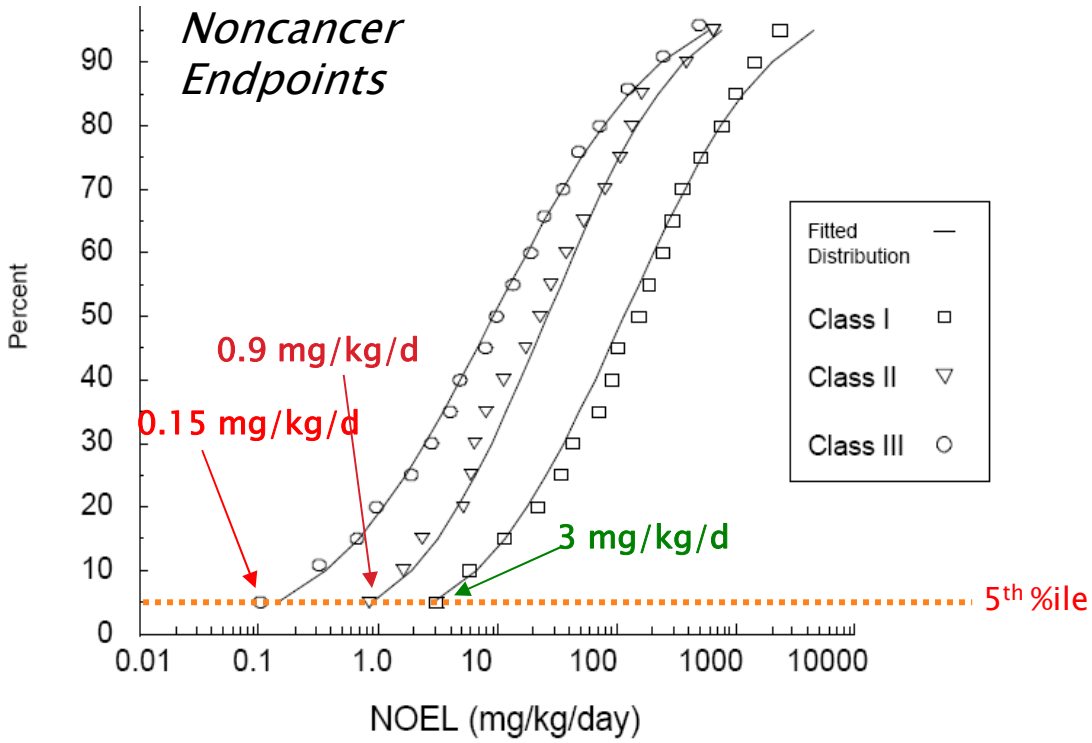
REDUCTION-REFINEMENT

Tier III: Refined *In vivo* tests to measure toxicity

Tier IV: in vivo tests

Why eco-TTCs?

- Established/useful concept in human health assessment



Benefits of eco-TTCs?

Screening-level hazard assessments

- Maximizes resource use (animals, time, $$)
- Potential for rapid-decision making
- Fully utilizes existing knowledge
- Allows evaluation of chemicals with little or no toxicity data
- Provides conservative estimates for low-production chemicals
- Supports read-across

Why now?

- Toxicology data is abundant and high-quality
- Increasing regulatory assessment needs
- Improved ability to probe complex chemical information / data

The Challenges

- All existing (non-human) species
- All environmental compartments
- Huge diversity of data
- Scattering of data sources
- Changes in methods over time
- Differences in regulatory schemes
- AMOUNT OF DATA

WHAT

Large, diverse datasets

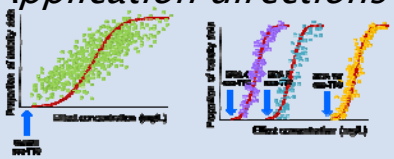
Organization, data quality, architecture

Assign to MOA, function, use, etc.

Classify as acute / chronic

Data analysis tools to derive distributions

Expert analysis
Application directions



Ecotox Data Collection

Data Harmonization / Curation

Data Characterization / Classification

EcoTTC DATABASE

Distribution Metric

Data Analysis / ecoTTC Derivation

HOW

'SIFT' Process

Access database development

MOA classification tools

Chemical classification tools

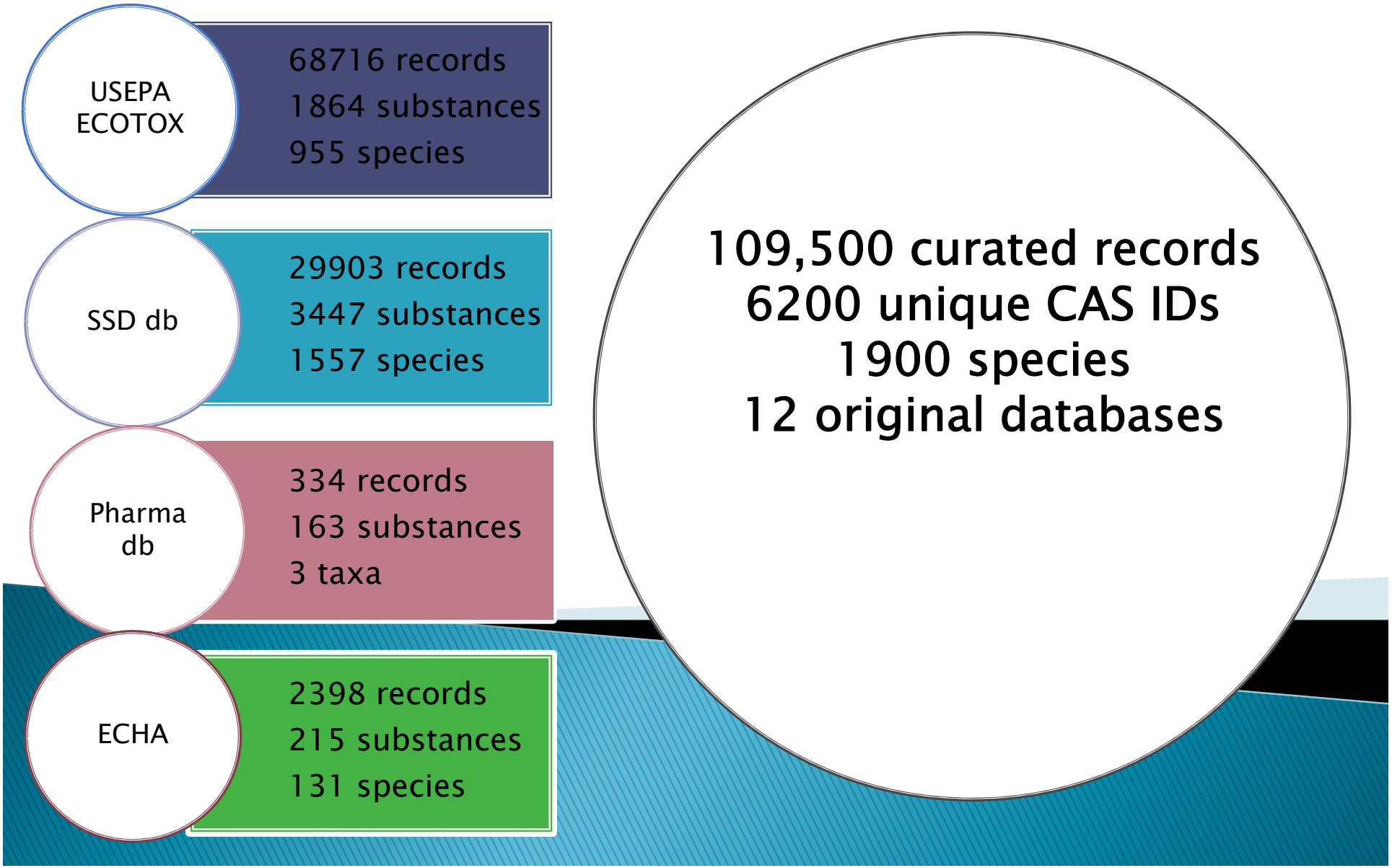
Acute / chronic logic tool

PNEC derivation tool

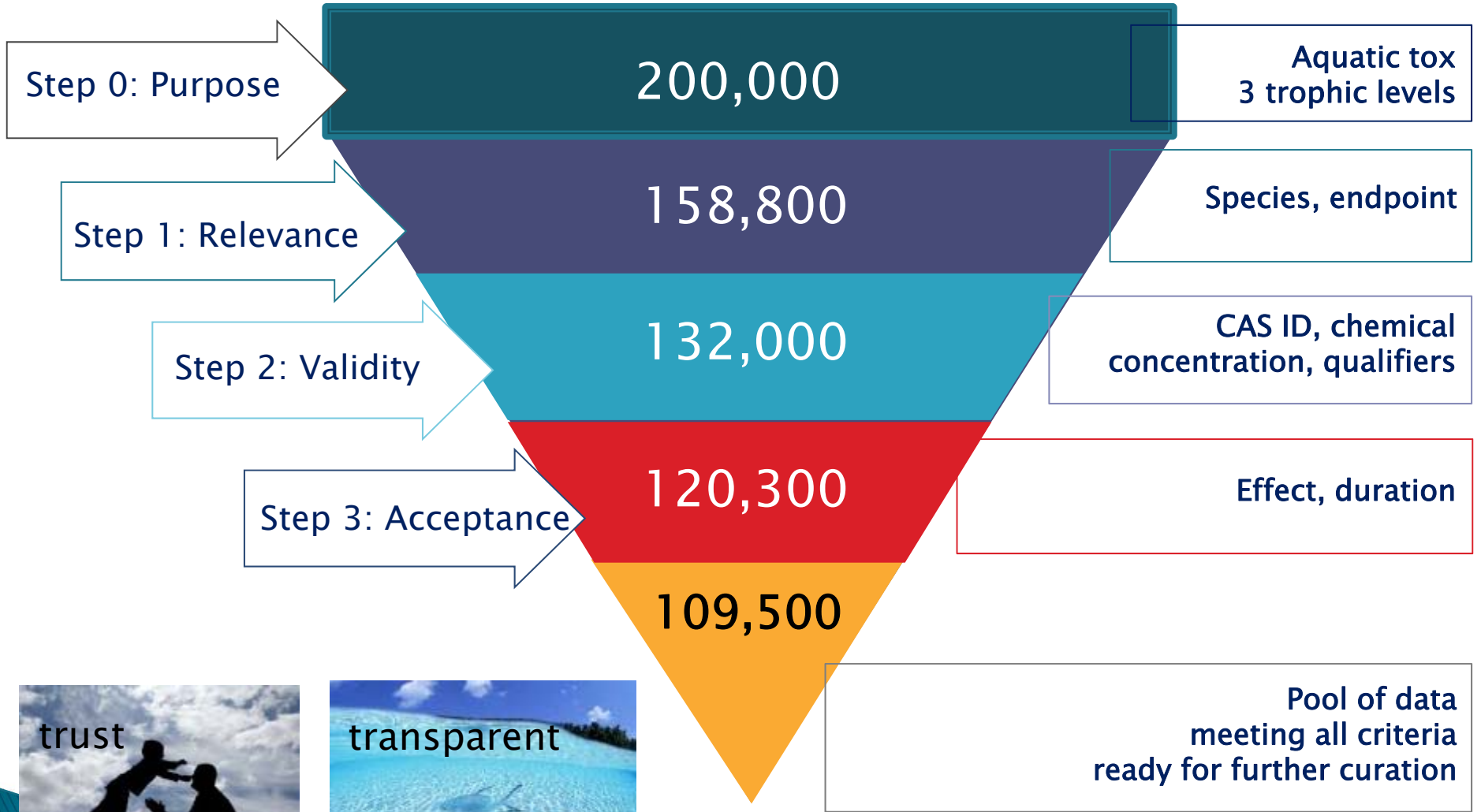
R tool for probability distributions

Threshold calculations

Database contents



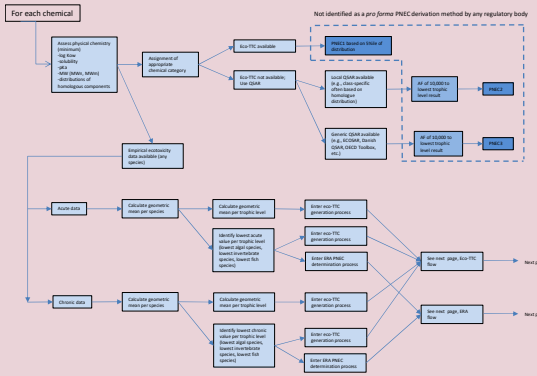
Data Harmonization / curation



Adapted from Beasley et al., 2015. Environ Toxicol Chem 34, 1436–1442

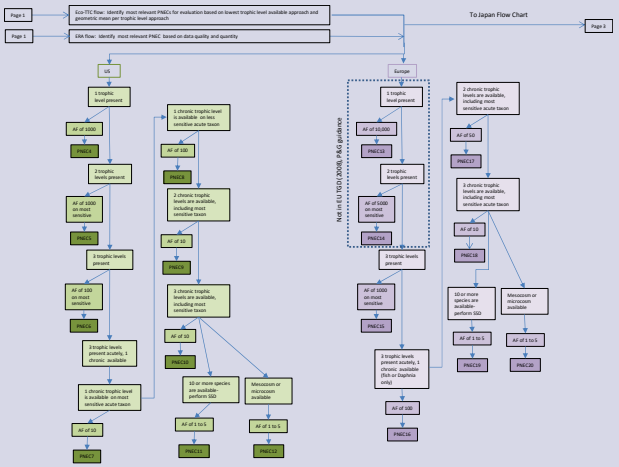
Programming Requires Explicit Logic Diagrams

Phys-chem/MOA

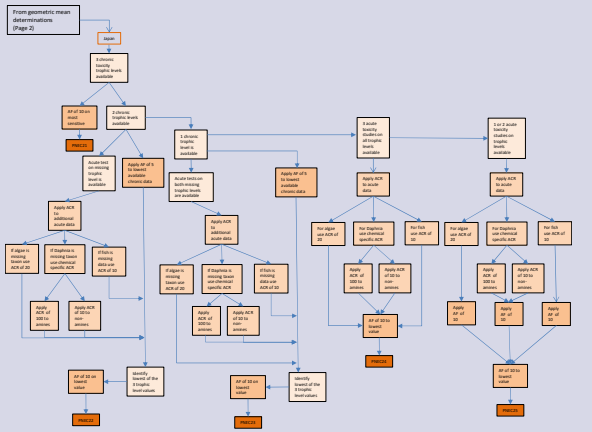


ERA Processes

US

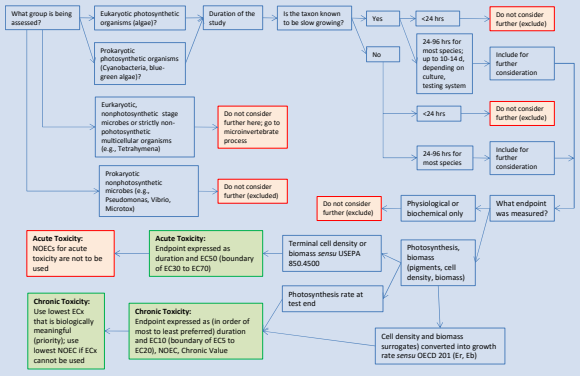


Japan

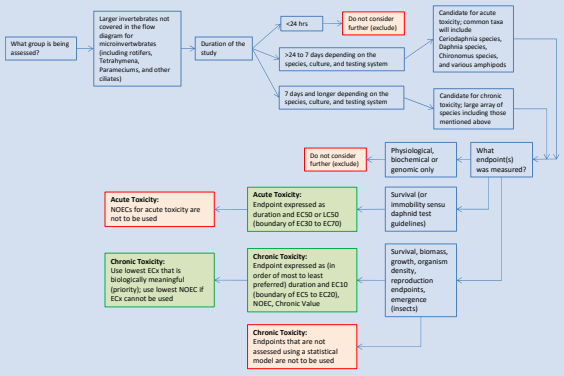


Acute and chronic toxicity

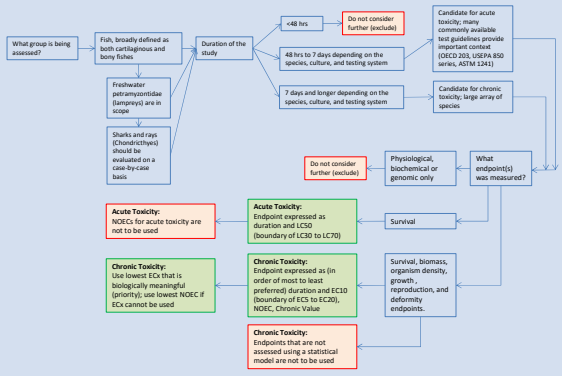
Microbes



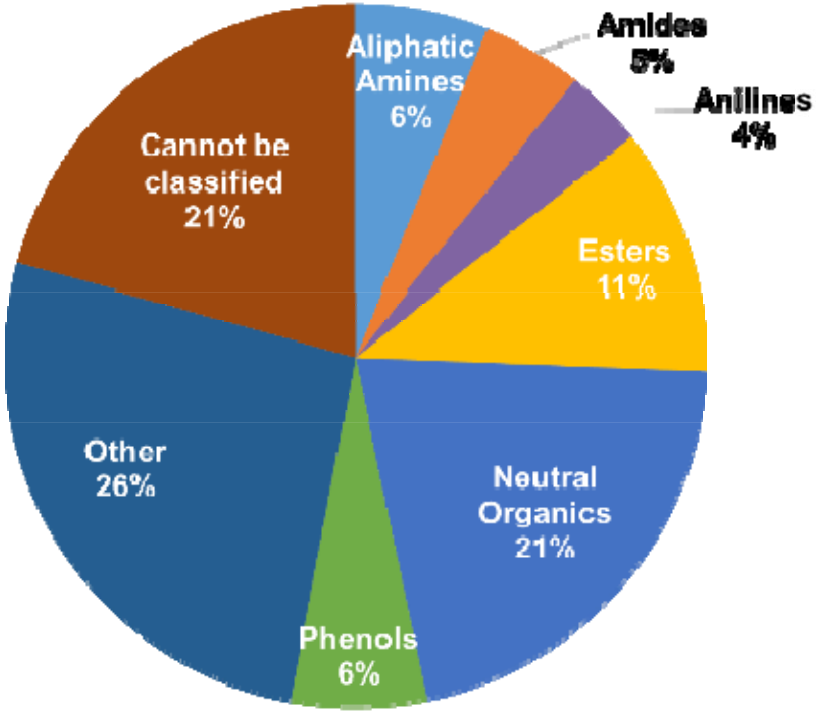
Macroinvertebrates



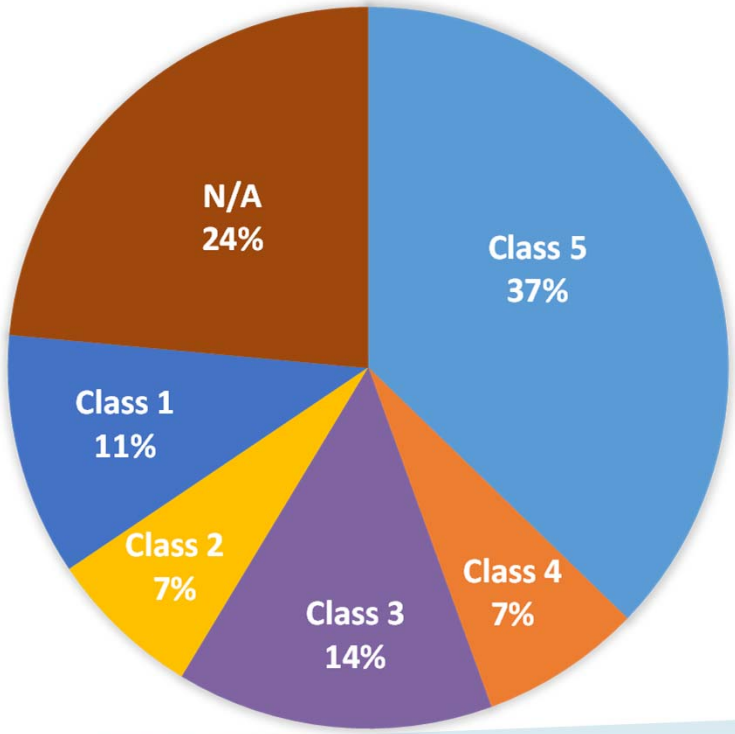
Fish



Data Characterization: Mode of action

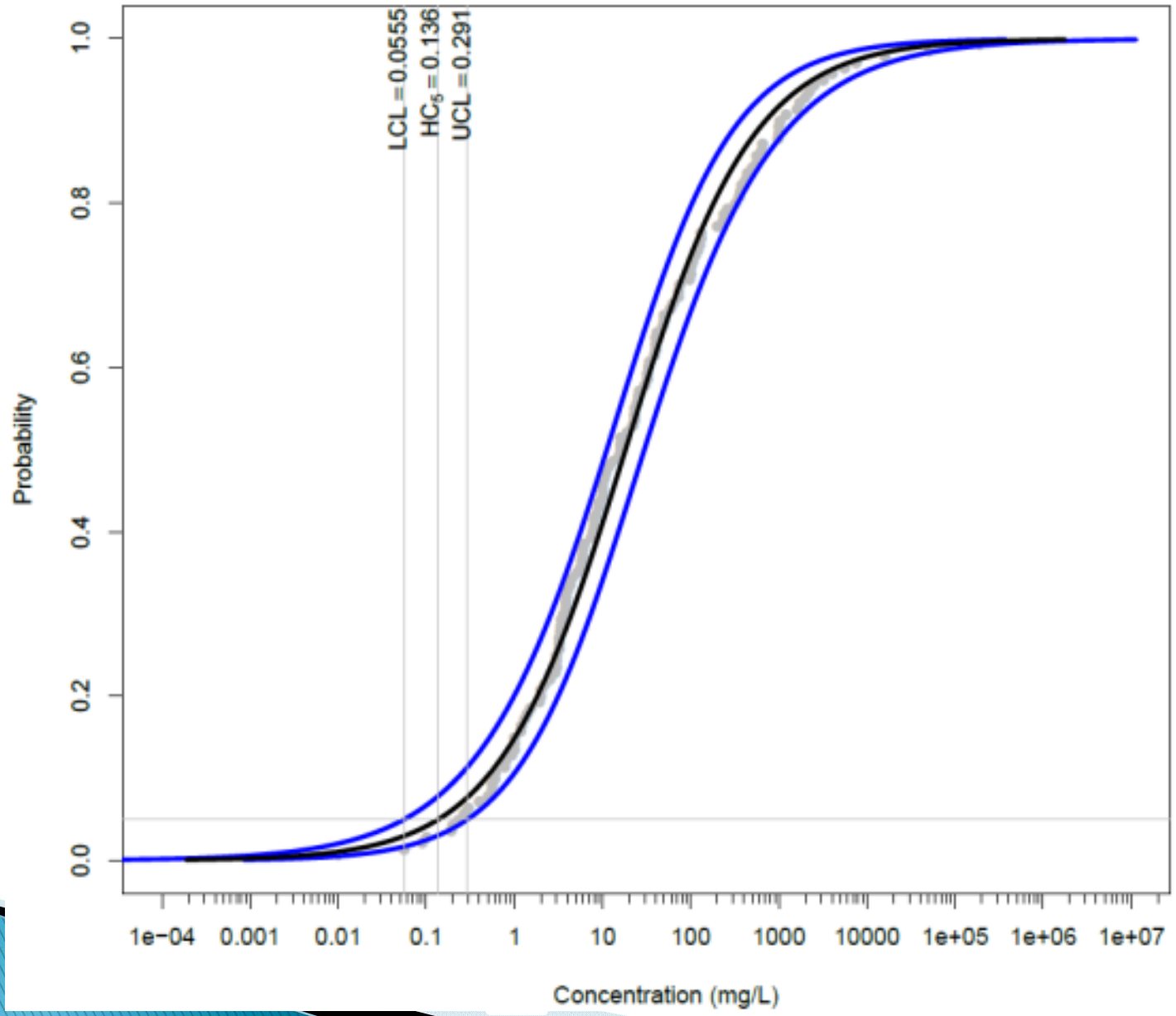


ECOSAR chemical classifications from the evaluated dataset (n=5636 unique CAS)



Verhaar MoA chemical classifications (n=5636 unique CAS)

Distributions



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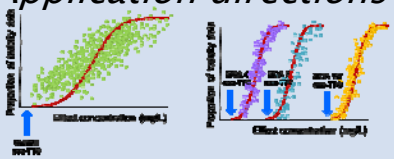

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MOA classification tools
Chemical classification tools
Acute / chronic logic tool

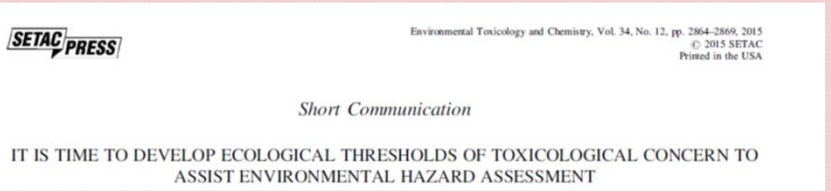
SQL database
Web-based user interface

PNEC derivation tool

R tool for probability distributions
Threshold calculations

Publications…..

Need for eco TTC



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Short Communication

IT IS TIME TO DEVELOP ECOLOGICAL THRESHOLDS OF TOXICOLOGICAL CONCERN TO ASSIST ENVIRONMENTAL HAZARD ASSESSMENT

Database

- Description of database structure
- Sources of data
- Filtering process
- Analysis of database content

PNEC derivation tool

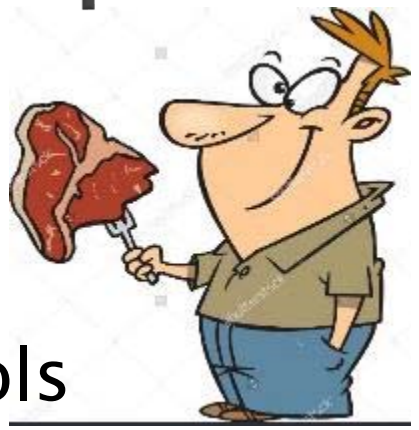
- Codify the options that can be used to evaluate ecotoxicity data using ecoTTC database
- Communicate differences/similarities in regulatory outcomes

Chemical classification

- Review of MOA assignment schemes
- Discussed tiered approach based on information
- Potentially describe what we used in ecoTTC databases (which are “most appropriate” to use”)

2017 Stakeholder Workshop

A new approach….



- eco TTC database and associated tools publicly available
- Workshop participants invited to develop case studies to evaluate the approach, database, and tools prior to the workshop
- Results from various stakeholder exercises will be presented and discussed